Claims

We claim:

1. A method for immunizing a host mammal to produce a population of monoclonal antibodies that bind to antigens representative of a specific cell type that are heterologous to the host mammal, comprising introducing into the mammal a plurality of viable and intact cells of said cell type, wherein the surfaces of the cells are free of serum.

2. The method for immunizing a mammal of claim 1, wherein the cells have been cultured in a serum-free medium.

3. The method for immunizing a mammal of claim 1, wherein the cells have been grown in the form of a monolayer.

4. The method for immunizing a mammal of claim 1, wherein the cells have been grown in the form of aggregates.

5. The method for immunizing a mammal of claim 1, wherein the cells have been grown on a biological or a non-biological substrate.

6. The method for immunizing a mammal of claim 5, wherein the biological substrate is selected from the group consisting of collagen, fibronectin, laminin, and poly-lysine.

7. The method for immunizing a mammal of claim 5, wherein the non-biological substrate is selected from the group consisting of nitrocellulose, nylon, and polytetrafluoroethylene membrane.

8. The method for immunizing a mammal of claim 1, wherein the cells are of embryonic or adult origin.

9. The method for immunizing a mammal of claim 1, wherein the cells are of ectodermal, or endodermal or mesodermal origin.

10. The method for immunizing a mammal of claim 1, wherein the cells are selected from the group consisting of ASC, ESC, ROG, BUD, RED, NODD, BR516, RL-65, and NEP cells.

11. A method of generating monoclonal antibodies binding to surface antigens of a specific cell type, comprising the steps of:

(a) immunizing a host mammal with a plurality of viable and intact cells of a specific cell type that are heterologous to the host mammal, wherein the surfaces of the cells are free of serum;

(b) fusing lymphoid cells from the immunized mammal with an immortalized cell line to produce hybridomas that secrete monoclonal antibodies;

(c) culturing the hybridomas under the conditions favorable for the secretion of monoclonal antibodies; and

(d) selecting the hybridomas that secrete monoclonal antibodies binding to surface antigens present on the viable and intact cells of step (a).

12. The method of generating monoclonal antibodies of claim 11, wherein the selection is effected by an immunoassay.

13. The method of generating monoclonal antibodies of claim 12, wherein the immunoassay is selected from the group consisting of ELISA and immunoblotting.

14. The method of generating monoclonal antibodies of claim 11, wherein the selection is effected by a cell sorting process.

15. The method of generating monoclonal antibodies of claim 14, wherein the cell sorting process is FACS.

16. The method of generating monoclonal antibodies of claim 11, wherein the monoclonal antibodies bind to the extracellular domain of the surface antigens.

17. The method of generating monoclonal antibodies of claim 11, wherein the cells have been cultured in a serum-free medium.

18. The method of generating monoclonal antibodies of claim 11, wherein the cells have been grown in the form of a monolayer.

19. The method of generating monoclonal antibodies of claim 11, wherein the cells have been grown in the form of aggregates.

20. The method of generating monoclonal antibodies of claim 11, wherein the cells have been grown on a biological or a non-biological substrate.

21. The method of generating monoclonal antibodies of claim 20, wherein the biological substrate is selected from the group consisting of collagen, fibronectin, laminin and poly-lysine.

22. The method of generating monoclonal antibodies of claim 20, wherein the non-biological substrate is selected from the group consisting of nitrocellulose, nylon, and polytetrafluoroethylene membrane.

23. The method of generating monoclonal antibodies of claim 11, wherein the cells are of embryonic or adult origin.

24. A population of monoclonal antibodies that lacks substantial immunological reactivity with serum biomolecules and contains at least one antibody reactive with an antigen that is tissue-selective, or sub-tissue selective, or cell-type specific.

25. A population of monoclonal antibodies generated by the method of claim 11.

26. The population of monoclonal antibodies of claim 25, wherein the monoclonal antibodies specifically bind to the extracellular domain of the cell surface antigens.

27. A population of hybridomas generated by the method of claim 11.

28. The population of hybridomas of claim 27, wherein the hybridomas produce monoclonal antibodies that specifically bind to the extracellular domain of the cell surface antigens.

29. A method of determining the combination of cell surface antigens present on a specific cell type, comprising the step of:

(a) immunizing a mammal with a plurality of viable and intact cells of a specific cell type that is heterologous to the host mammal, wherein the surfaces of the cells are free of serum;

(b) fusing lymphoid cells from the immunized mammal with an immortalized cell line to produce hybridomas that secrete monoclonal antibodies;

(c) culturing the hybridomas under the conditions favorable for the secretion of monoclonal antibodies;

(d) selecting the hybridomas that secrete monoclonal antibodies binding to the cell surface antigens present on the viable and intact cells of step (a); and

(e) identifying the antigens to which the monoclonal antibodies bind, and thereby determining the combination of cell surface antigens present on said specific cell type.

30. The method of claim 29, wherein identifying the antigens of step (e) further comprises obtaining cDNAs of the specific cell type, expressing the cDNAs in a second cell type at a level of at least 5 fold higher than that of the corresponding endogenous antigens, if present, and screen cells of the second cell type for a specific binding to the monoclonal antibodies secreted by the hybridomas identified in (d).